K072358

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OCT 31 2007

BIOPLEX 2200 VASCULITIS KIT, CALIBRATORS AND CONTROLS 510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

510(k) Number	510(k) Summary Report Date
K072358	October 24, 2007

MANUFACTURER INFORMATION

Manufacturer	
Manufacturer Address	Bio-Rad Laboratories, Inc. Clinical Systems Division 4000 Alfred Nobel Drive Hercules, CA 94547
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Establishment Registration No.	2915274
Owner / Operator	Bio-Rad Laboratories, Inc. 4000 Alfred Nobel Drive Hercules, CA 94547
Owner / Operator No.	9929003
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CLASSIFICATION INFORMATION

Classification Name	Test System, Antineutrophil Cytoplasmic Antibodies (ANCA), Devices, Measure, Antibodies to Glomerular Basement Membrane (GBM)
Common Name:	Multi-Analyte Detection System Vasculitis
Product Trade Name	BioPlex 2200 Vasculitis kit on the BioPlex 2200 Multi-Analyte Detection System BioPlex 2200 Vasculitis Calibrator Set BioPlex 2200 Vasculitis Control Set
Device Class	Class II
Classification Panel	Immunology
Regulation Number	866.5660-Multiple Autoantibodies Immunological Test System

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LEGALLY MARKETED EQUIVALENT (SE) DEVICES

Comparative FDA Cleared PREDICATE DEVICE	510(k) Number	Decision Date
Phadia Varelisa™ MPO EIA	K041040	06/16/04
Phadia Varelisa™ PR3 EIA	K041043	07/02/04
INOVA QUANTA Lite™ GBM ELISA	K984336	02/08/99
INOVA NOVA Lite ANCA (Ethanol-fixed Slides)	K961340	07/10/96

DEVICE DESCRIPTION

The Vasculitis kit uses multiplex flow immunoassay, a methodology that greatly resembles traditional EIA, but permits simultaneous detection and identification of many antibodies in a single tube. Three (3) different populations of beads are coated with antigens associated with vasculitis disease (MPO, PR3 and GBM).The BioPlex 2200 System combines an aliquot of patient sample, sample diluent, and bead reagent into a reaction vessel. The mixture is incubated at 37°C. After a wash cycle, anti-human IgG antibody, conjugated to phycoerythrin (PE), is added to the dyed beads and this mixture is incubated at 37°C. The excess conjugate is removed in another wash cycle, and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes, and the amount of antibody captured by the antigen is determined by the fluorescence of the attached PE. Raw data is calculated in relative fluorescence intensity (RFI).

Three additional dyed beads, an Internal Standard Bead (ISB), a Serum Verification Bead (SVB) and a Reagent Blank Bead (RBB) are present in each reaction mixture to verify detector response, the addition of serum or plasma to the reaction vessel and the absence of significant non-specific binding in serum or plasma. Refer to the BioPlex 2200 System Operation Manual for more information.

The instrument is calibrated using a set of four (4) distinct calibrator vials, supplied separately by Bio-Rad Laboratories. A combination of four (4) vials representing four (4) different antibody concentrations are used for semi-quantitative calibration. The result for each of these antibodies is expressed as an antibody index (AI).

KIT COMPONENTS

BioPlex 2200 Vasculitis reagent pack (Catalog No. 665-1850). The reagent pack contains supplies sufficient for 100 tests.

Vial	Description
Bead Set	One (1) 10 mL vial, containing dyed beads coated with Myeloperoxidase (MPO), Proteinase-3 (PR3) and Glomerular Basement Membrane (GBM); an Internal Standard bead (ISB), a Serum Verification bead (SVB), and a Reagent Blank bead (RBB) in a MOPS (3-[N-Morpholino] propanesulfonic acid) buffer supplemented with Glycerol and protein stabilizers (bovine). ProClin® 300 (0.3%), sodium benzoate (0.1%) and sodium azide (<0.1%) are added as preservatives.

Conjugate CONJ	One (1) 5 mL vial, containing phycoerythrin conjugated murine monoclonal anti-human IgG and phycoerythrin conjugated murine monoclonal anti-human FXIII in phosphate buffer supplemented with murine and bovine protein stabilizers. ProClin® 300 (0.3%), sodium benzoate (0.1%) and sodium azide (<0.1%) are added as preservatives.
Sample Diluent	One (1) 10 mL vial, containing bovine and murine protein stabilizers in triethanolamine buffer. ProClin® 300 (0.3%), sodium benzoate (0.1%) and sodium azide (<0.1%) are added as preservatives.

ADDITIONAL REQUIRED ITEMS, AVAILABLE FROM BIO-RAD

	Description
663-1800	BioPlex 2200 Vasculitis Calibrator Set: Four (4) 500 µL vials, each containing human antibodies to MPO, PR3 and GBM, in a human serum matrix made from defibrinated plasma. All calibrators contain ProClin® 300 (0.3%), sodium benzoate (0.1%) and sodium azide (<0.1%) as preservatives.
663-1830	BioPlex 2200 Vasculitis Control Set: Two (2) 1.5 mL Positive Control serum vials, each containing human antibodies to MPO, PR3 and GBM, in a human serum matrix made from defibrinated plasma; and two (2) 1.5 mL Negative Control serum vials, in a human serum matrix made from defibrinated plasma. All controls contain ProClin® 300 (0.3%), sodium benzoate (0.1%) and sodium azide (<0.1%) as preservatives.
660-0817	BioPlex 2200 Sheath Fluid: Two (2) 4 L bottles containing Phosphate Buffered Saline (PBS). ProClin® 300 (0.03%) and sodium azide (<0.1%) are added as preservatives.
660-0818	BioPlex 2200 Wash Solution: One (1) 10 L bottle containing Phosphate Buffered Saline (PBS) and Tween 20. ProClin® 300 (0.03%) and sodium azide (<0.1%) are added as preservatives.
660-0000	BioPlex 2200 Instrument and Software System

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INTENDED USE

BioPlex™ 2200 Vasculitis Kit

The BioPlex™ 2200 Vasculitis kit is a multiplex flow immunoassay intended for the semi-quantitative detection of IgG autoantibodies to Myeloperoxidase (MPO), Proteinase 3 (PR3) and Glomerular Basement Membrane (GBM) in human serum. In conjunction with clinical findings, the test system is used as an aid in the diagnosis of anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitides: Microscopic Polyangiitis (MPA), Necrotising Glomerulonephritis, Churg-Strauss Syndrome, Wegener's Granulomatosis and the autoimmune renal disorder, Goodpasture's syndrome.

The BioPlex 2200 Vasculitis kit is intended for use with the Bio-Rad BioPlex 2200 System.

BioPlex 2200 Vasculitis Calibrator Set

The BioPlex 2200 Vasculitis Calibrator Set is intended for the calibration of the BioPlex 2200 Vasculitis Reagent Pack.

BioPlex 2200 Vasculitis Control Set

The BioPlex 2200 Vasculitis Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 Instrument and BioPlex 2200 Vasculitis Reagent Pack in the clinical laboratory. The performance of the BioPlex 2200 Vasculitis Control Set has not been established with any other Vasculitis assays.

INDICATIONS FOR USE

The BioPlex 2200 Vasculitis kit is a multiplex flow immunoassay intended for the semi-quantitative detection of IgG autoantibodies to Myeloperoxidase (MPO), serine proteinase 3 (PR3) and Glomerular Basement Membrane (GBM) in human serum.

The BioPlex 2200 Vasculitis kit is intended for use with the Bio-Rad BioPlex 2200 System.

Uses:

The test system is used to detect the presence of antibodies in serum samples, as an aid in the diagnosis of certain autoimmune vasculitides such as Microscopic Polyangiitis (MPA), Necrotising Glomerulonephritis, Churg-Strauss Syndrome, Wegener's Granulomatosis and autoimmune renal disorders, such as Goodpasture's syndrome, in conjunction with clinical findings and other laboratory tests.

TECHNOLOGICAL CHARACTERISTICS

The following tables summarize similarities and differences between the BioPlex 2200 Vasculitis Kit and the predicate devices used in comparative studies with the BioPlex 2200 Vasculitis Kit.

A. BioPlex 2200 Vasculitis vs. Predicate Phadia Varelisa MPO ANCA EIA

Table 1: Similarities between reagents and materials

Similarities between Components / Materials	BioPlex 2200 Vasculitis	Predicate Phadia Varelisa MPO ANCA EIA
Reagents	Wash Buffer, Sample Diluent	Wash Buffer, Serum Diluent

Calibrators	Calibrators	Calibrators
Controls	Negative Control and Multi-Analyte Positive Control (MPO, PR3 and GBM)	Negative Control, Positive Control

Table 2: Similarities between reagents with regard to function and use

Similarities between Function and Use	**BioPlex 2200 Vasculitis**	**Predicate Phadia Varelisa MPO ANCA EIA**
Intended Use	Semi-quantitative detection of IgG autoantibodies to MPO, PR3 and GBM in human serum.	Semi-quantitative and qualitative determination of MPO Anti neutrophil cytoplasmic antibodies in human serum or plasma.
Matrices	Serum	Serum

Table 3: Differences between reagents and materials

Differences between Components / Materials	**BioPlex 2200 Vasculitis**	**Predicate Phadia Varelisa MPO ANCA EIA**
Solid Phase	Bead reagent - dyed antigen coated beads	96 well microplate – antigen coated microwells
Reagents	Conjugate: Anti-human IgG / Phycoerythrin	Conjugate: Anti-human IgG HRP conjugate/Substrate (TMB)
Sheath Fluid	Sheath Fluid is used to suspend the bead reagent and introduce it into the detector.	Not similar; not utilized in EIA's

Table 4: Differences between reagents with regard to function and use

Differences between Function and Use	**BioPlex 2200 Vasculitis**	**Predicate Phadia Varelisa MPO ANCA EIA**
Analyte Detection	Multi-Analyte Detection (human IgG autoantibodies to MPO, PR3 and GBM)	Single Analyte Detection (Human IgG antibodies to MPO)
Matrices	Serum	Plasma

B. BioPlex 2200 Vasculitis vs. Predicate Phadia Varelisa PR3 ANCA EIA

Table 5: Similarities between reagents and materials

Similarities between Components / Materials	**BioPlex 2200 Vasculitis**	**Predicate Phadia Varelisa PR3 ANCA EIA**
Reagents	Wash Buffer, Sample Diluent	Wash Buffer, Sample Diluent
Calibrators	Calibrators	Calibrators
Controls	Negative Control and Multi-Analyte Positive Control (MPO, PR3 and GBM)	Negative Control, Positive Control

Table 6: Similarities between reagents with regard to function and use

Similarities between Components / Materials	BioPlex 2200 Vasculitis	Predicate Phadia Varelisa PR3 ANCA EIA
Intended Use	Semi-quantitative detection of IgG autoantibodies to MPO, PR3 and GBM in human serum.	Semi-quantitative and qualitative determination of PR3 Anti neutrophil cytoplasmic antibodies in human serum or plasma.
Matrices	Serum	Serum

Table 7: Differences between reagents and materials

Differences between Components / Materials	BioPlex 2200 Vasculitis	Predicate Phadia Varelisa PR3 ANCA EIA
Solid Phase	Bead reagent - dyed antigen coated beads	96 well microplate – antigen coated microwells
Reagents	Conjugate: Anti-human IgG / Phycoerythrin	Conjugate: Anti-Human IgG HRP Conjugate /Substrate (TMB)
Sheath Fluid	Sheath Fluid is used to suspend the bead reagent and introduce it into the detector.	Not similar; not utilized in EIA's.

Table 8: Differences between reagents with regard to function and use

Differences between Function and Use	BioPlex 2200 Vasculitis	Predicate Phadia Varelisa PR3 ANCA EIA
Analyte Detection	Multi-Analyte Detection (human IgG autoantibodies to MPO, PR3 and GBM)	Single Analyte Detection (Human IgG antibodies to PR3)
Matrices	Serum	Plasma

C. BioPlex 2200 Vasculitis vs. Predicate INOVA QUANTA-Lite GBM ELISA

Table 9: Similarities between reagents and materials

Similarities between Components / Materials	BioPlex 2200 Vasculitis	Predicate INOVA QUANTA-Lite GBM ELISA
Reagents	Wash Buffer, Sample Diluent	Wash Buffer, Serum Diluent
Controls	Negative Control and Multi-Analyte Positive Control (MPO, PR3 and GBM)	Negative Control, Positive Control

Table 10: Similarities between reagents with regard to function and use

Similarities between Components / Materials	BioPlex 2200 Vasculitis	Predicate INOVA QUANTA-Lite GBM ELISA
Intended Use	Semi-quantitative detection of IgG autoantibodies to MPO, PR3 and GBM in human serum.	Semi-quantitative determination of anti neutrophil cytoplasmic antibodies to GBM in human serum

Table 11: Differences between reagents and materials

Differences between Components / Materials	BioPlex 2200 Vasculitis	Predicate INOVA QUANTA-Lite GBM ELISA
Solid Phase	Bead reagent - dyed antigen coated beads	96 well microplate – antigen coated microwells

Reagents	Conjugate: Anti-human IgG / Phycoerythrin	Conjugate: Anti-Human IgG / Horse-radish Peroxidase, Substrate (TMB)
Sheath Fluid	Sheath Fluid is used to suspend the bead reagent and introduce it into the detector	Not similar; not utilized in EIA's.
Calibrators	Calibrators	None

Table 12: Differences between reagents with regard to function and use

Differences between Function and Use	**BioPlex 2200 Vasculitis**	**Predicate INOVA QUANTA-Lite GBM ELISA**
Analyte Detection	Multi-Analyte Detection (human IgG autoantibodies to MPO, PR3 and GBM)	Single Analyte Detection (Human IgG antibodies to GBM)

D. BioPlex 2200 Vasculitis vs. Predicate INOVA NOVA Lite, ANCA, Ethanol Fixed Slides

Table 13: Similarities between reagents and materials

Similarities between Components / Materials	**BioPlex 2200 Vasculitis**	**Predicate INOVA NOVA Lite, ANCA, Ethanol Fixed Slides**
Controls	Negative Control and Multi-Analyte Positive Control (MPO, PR3 and GBM)	IFA Negative Control, p-ANCA Positive Control, c-ANCA Positive Control

Table 14: Similarities between reagents with regard to function and use

Similarities between Components / Materials	**BioPlex 2200 Vasculitis**	**Predicate INOVA NOVA Lite, ANCA, Ethanol Fixed Slides**
Intended Use	Semi-quantitative detection of IgG autoantibodies to MPO, PR3 and GBM in human serum.	Semi-quantitative determination of Anti neutrophil cytoplasmic antibodies in human serum.
Matrices	Serum	Serum

Table 15: Differences between reagents and materials

Differences between Components / Materials	**BioPlex 2200 Vasculitis**	**Predicate INOVA NOVA Lite, ANCA, Ethanol Fixed Slides**
Solid Phase	Bead reagent - dyed antigen coated beads	ANCA, Ethanol fixed neutrophils Substrate slides
Reagents	Conjugate: Anti-human IgG / Phycoerythrin	Conjugate: Anti-Human IgG / Horse-radish Peroxidase
Sheath Fluid	Sheath Fluid is used to suspend the bead reagent and introduce it into the detector.	Not similar; not utilized in EIA's.
Calibrators	Calibrators	None

Table 16: Differences between reagents with regard to function and use

Differences between Function and Use	**BioPlex 2200 Vasculitis**	**Predicate INOVA NOVA Lite, ANCA, Ethanol Fixed Slides**
Analyte Detection	Multi-Analyte Detection (human IgG autoantibodies to MPO, PR3 and GBM)	Single Analyte Detection (Human IgG antibodies)

Solid Phase	Bead reagent - dyed antigen coated beads	ANCA, Ethanol fixed neutrophils Substrate slides

PERFORMANCE SUMMARY

A. Expected Values

Expected values for the BioPlex 2200 Vasculitis kit are presented in the following tables for serum samples from normal blood donors (N=293) and unselected patient samples previously tested with vasculitis tests (N=300). A total of 300 serum samples from the normal blood donor population were tested. Seven (7) samples from the normal blood donor population were excluded due to "Serum Verification Bead (SVB) signal too low" analysis error messages during BioPlex 2200 Vasculitis kit testing. For all analytes, results of <1.0 AI are negative and results of 1.0 AI or greater are reported as positive.

Table A. BioPlex 2200 Vasculitis Kit – Normal Blood Donors (N=293)

BioPlex Result	Positive # (%)	Negative # (%)
Anti-MPO	0/293 (0.0%)	293/293 (100.0%)
Anti-PR3	0/293 (0.0%)	293/293 (100.0%)
Anti-GBM	2/293 (0.7%)	291/293 (99.3%)

Table B. BioPlex 2200 Vasculitis Kit – Unselected Patient Samples Previously Tested With Vasculitis Tests (N=300)

BioPlex Result	Positive # (%)	Negative # (%)
Anti-MPO	14/300 (4.7%)	286/300 (95.3%)
Anti-PR3	8/300 (2.7%)	292/300 (97.3%)
Anti-GBM	1/300 (0.3%)	299/300 (99.7%)

B. Reproducibility Studies

A reproducibility panel, consisting of ten (10) serum panel members, was prepared by Bio-Rad Laboratories. The positive panel members were prepared by combining patient samples positive for

antibodies to MPO, PR3 and GBM. Two (2) of the ten (10) had high levels of the antibodies to MPO, PR3 and GBM; two (2) members had low levels of the antibodies to MPO, PR3 and GBM; and two (2) members had antibody levels near the cutoff. There was also one (1) high negative and one (1) low negative panel member. In addition, a BioPlex 2200 Vasculitis positive control (antibody positive for MPO, PR3 and GBM) and a negative control (antibody negative for all 3 analytes) were included and tested as panel members.

Reproducibility testing was performed at two (2) US testing facilities and an internal site (Bio-Rad Laboratories) on a total of two (2) lots of the BioPlex 2200 Vasculitis kit. The ten (10) panel members were provided to the each of the testing sites. Two (2) of the three (3) testing facilities evaluated reproducibility using one (1) kit lot of the BioPlex 2200 Vasculitis kit and the third site evaluated the second lot of the BioPlex 2200 Vasculitis kit. Each of the ten (10) panel members was tested in duplicate (x2) on two runs per day for three days at each testing site (2 times x 2 runs x 3 days x 3 sites = 36 replicates per panel member and controls). The data were then analyzed for intra assay and inter-assay reproducibility according to the Clinical and Laboratory Standards Institute guidance (formerly NCCLS) EP5-A2, revised November 2004 and ISO/TR 22971:2005. The mean Antibody Index (AI), standard deviation (SD), and percent coefficient of variation (%CV) for each panel member were calculated. Results can be found in the below table:

Table. Reproducibility; BioPlex 2200 Vasculitis

Vasculitis Kit Panel Members		BioPlex 2200 Vasculitis Kit											
		Sample N	Mean AI	Within-Run		Between-Run		Between-Day		Between-Site*		Total	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Vasculitis Anti-MPO	High Positive 1	36	4.0	0.277	7.0%	0.156	3.9%	0.022	0.6%	0.326	8.2%	0.456	11.5 %
	High Positive 2	36	5.5	0.295	5.4%	0.249	4.5%	0.000	0.0%	0.254	4.6%	0.462	8.4%
	Low Positive 1	36	1.5	0.065	4.4%	0.041	2.8%	0.043	3.0%	0.017	1.2%	0.089	6.2%
	Low Positive 2	36	1.9	0.169	8.6%	0.000	0.0%	0.000	0.0%	0.025	1.3%	0.170	8.7%
	Near	36	1.0	0.058	5.6%	0.000	0.0%	0.032	3.1%	0.048	4.6%	0.082	7.9%

	Cutoff 1												
	Near Cutoff 2	36	1.3	0.053	3.9%	0.033	2.5%	0.041	3.1%	0.000	0.0%	0.075	5.6%
	Positive Control	36	2.9	0.198	6.8%	0.000	0.0%	0.000	0.0%	0.102	3.5%	0.223	7.7%
	Negative Control	36	0.2	0.000	0.0%	0.000	0.0%	0.000	0.0%	0.000	0.0%	0.000	0.0%
Vasculitis Anti-PR3	High Positive 1	36	4.2	0.301	7.2%	0.000	0.0%	0.101	2.4%	0.076	1.8%	0.326	7.8%
	High Positive 2	36	4.5	0.171	3.8%	0.202	4.5%	0.000	0.0%	0.267	6.0%	0.376	8.4%
	Low Positive 1	36	1.4	0.067	4.9%	0.024	1.7%	0.075	5.5%	0.033	2.4%	0.108	7.9%
	Low Positive 2	36	1.5	0.128	8.3%	0.032	2.1%	0.000	0.0%	0.085	5.5%	0.157	10.2 %
	Near Cutoff 1	36	1.2	0.062	5.1%	0.000	0.0%	0.057	4.7%	0.027	2.2%	0.088	7.3%
	Near Cutoff 2	36	1.1	0.053	4.7%	0.024	2.1%	0.045	3.9%	0.000	0.0%	0.073	6.4%
	Positive Control	36	2.3	0.134	5.8%	0.000	0.0%	0.095	4.1%	0.032	1.4%	0.167	7.3%
	Negative Control	36	0.2	0.019	8.9%	0.000	0.0%	0.027	12.6 %	0.024	10.9 %	0.041	18.8 %

Vasculitis Anti-GBM	High Positive 1	36	4.3	0.249	5.8%	0.000	0.0%	0.000	0.0%	0.204	4.7%	0.322	7.5%
	High Positive 2	36	4.8	0.162	3.4%	0.194	4.1%	0.000	0.0%	0.280	5.9%	0.377	7.9%
	Low Positive 1	36	1.4	0.081	5.6%	0.000	0.0%	0.064	4.5%	0.087	6.0%	0.135	9.4%
	Low Positive 2	36	1.7	0.093	5.5%	0.052	3.1%	0.000	0.0%	0.047	2.8%	0.116	6.9%
	Near Cutoff 1	36	1.1	0.037	3.4%	0.045	4.1%	0.000	0.0%	0.079	7.2%	0.099	9.0%
	Near Cutoff 2	36	1.2	0.060	5.0%	0.041	3.4%	0.017	1.4%	0.081	6.7%	0.110	9.2%
	Positive Control	36	2.8	0.139	4.9%	0.000	0.0%	0.000	0.0%	0.063	2.3%	0.153	5.4%
	Negative Control	36	0.2	0.000	0.0%	0.000	0.0%	0.000	0.0%	0.000	0.0%	0.000	0.0%

** Between-site variance includes between lot variance*

C. Comparative Testing

Three hundred (300) normal blood donors and three hundred (300) unselected patient samples previously tested with vasculitis tests were tested with the BioPlex 2200 Vasculitis kit. Seven (7) of the three hundred (300) normal blood donor samples were excluded due to "Serum Verification Bead (SVB) signal too low" analysis error during BioPlex 2200 Vasculitis kit testing. All samples were also tested by the corresponding commercially available microplate EIA methods. The results can be observed in Tables A - F.

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Table A. BioPlex 2200 vs. Anti-MPO EIA – Normal Blood Donors (N=293)

		BioPlex 2200 Vasculitis Anti-MPO Result								
		Positive	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
EIA Result	Positive	0	0	0	N/A	N/A	100.0% (293/293)	98.7%, 100%	100.0% (293/293)	98.7%, 100%
	Equivocal	0	0	0						
	Negative	0	293	293						
	Total	0	293	293						

N/A = Not Applicable

Table B. BioPlex 2200 vs. Anti-PR3 EIA – Normal Blood Donors (N=293)

		BioPlex 2200 Vasculitis Anti-PR3 Result								
		Positive	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
EIA Result	Positive	0	0	0	N/A	N/A	100.0% (293/293)	98.7%, 100%	100.0% (293/293)	98.7%, 100%
	Equivocal	0	0	0						
	Negative	0	293	293						
	Total	0	293	293						

N/A = Not Applicable

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Table C. BioPlex 2200 vs. Anti-GBM EIA – Normal Blood Donors (N=293)

		BioPlex 2200 Vasculitis Anti-GBM Result								
		Positive	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
EIA Result	Positive	0	2*	2	N/A	N/A	99.3% (289/291)	97.5%, 99.8%	98.6% (289/293)	96.5%, 99.5%
	Negative	2	289	291						
	Total	2	291	293						

** Two (2) positive anti-GBM EIA results were weak positive.*
N/A = Not Applicable

Table D. BioPlex 2200 vs. Anti-MPO EIA – Unselected Patient Samples Previously Tested With Vasculitis Tests (N=300)

		BioPlex 2200 Vasculitis Anti-MPO Result								
		Positive	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
EIA Result	Positive	5	2	7	71.4% (5/7)	35.9%, 91.8%	97.6% (284/291)	95.1%, 98.8%	96.3% (289/300)	93.6%, 97.9%
	Equivocal*	2	0	2						
	Negative	7	284	291						
	Total	14	286	300						

** Two (2) anti-MPO EIA equivocal results are included in the Overall Agreement.*

Table E. BioPlex 2200 vs. Anti-PR3 EIA – Unselected Patient Samples Previously Tested With Vasculitis Tests (N=300)

		BioPlex 2200 Vasculitis Anti-PR3 Result								
		Positive	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
EIA Result	Positive	5	0	5	100.0% (5/5)	56.5%, 100%	99.0% (292/295)	97%, 99.7%	99.0% (297/300)	97.1%, 99.7%
	Equivocal	0	0	0						
	Negative	3	292	295						
	Total	8	292	300						

Table F. BioPlex 2200 vs. Anti-GBM EIA – Unselected Patient Samples Previously Tested With Vasculitis Tests (N=300)

		BioPlex 2200 Vasculitis Anti-GBM Result								
		Positive	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
EIA Result	Positive	0	1*	1	Not Accurate (0/1)	Not Accurate	99.7% (298/299)	98.1%, 99.9%	99.3% (298/300)	97.6%, 99.8%
	Negative	1	298	299						
	Total	1	299	300						

** One (1) anti-GBM EIA results was a weak positive.*

The BioPlex 2200 Vasculitis kit was further evaluated by testing 227 retrospective samples positive for anti-MPO (N=100), anti-PR3 (N=100), and anti-GBM (N=27). All samples were also tested by the corresponding commercially available microplate EIA methods. In addition, the anti-MPO and anti-PR3 positive samples were tested by an ANCA IFA method using ethanol-fixed slides. The

results can be observed in Tables G - K.

Table G. BioPlex 2200 vs. Anti-MPO EIA – Retrospective Anti-MPO Positive Samples (N=100)

		BioPlex 2200 Vasculitis Anti-MPO Result								
		Positive	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
EIA Result	Positive	92	6	98	93.9% (92/98)	87.3%, 97.2%	N/A	N/A	93.0% (93/100)	86.2%, 96.6%
	Equivocal*	1	0	1						
	Negative	0	1	1						
	Total	93	7	100						

* *One (1) anti-MPO EIA equivocal result is included in the Overall Agreement.*
N/A = Not Applicable

Table H. BioPlex 2200 vs. Anti-PR3 EIA – Retrospective Anti-PR3 Positive Samples (N=100)

		BioPlex 2200 Vasculitis Anti-PR3 Result								
		Positive	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
EIA Result	Positive	79	0	79	100.0% (79/79)	95.4%, 100%	N/A	N/A	83.0% (83/100)	74.4%, 89.1%
	Equivocal*	9	1	10						
	Negative	7	4	11						
	Total	95	5	100						

* *Ten (10) anti-PR3 EIA equivocal results are included in the Overall Agreement.*
* *N/A = Not Applicable*

Table I. BioPlex 2200 vs. Anti-GBM EIA – Retrospective Anti-GBM Positive Samples (N=27)

		BioPlex 2200 Vasculitis Anti-GBM Result								
		Positive	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
EIA Result	Positive	16*	2**	18	88.9% (16/18)	67.2%, 96.9%	N/A	N/A	92.6% (25/27)	76.6%, 97.9%
	Negative	0	9	9						
	Total	16	11	27						

**Two (2) of the sixteen (16) anti-GBM EIA positive results were weak positive.*

*** One (1) of the two (2) anti-GBM EIA positive results were weak positive.*

The remaining fifteen (15) of the eighteen (18) anti-GBM EIA results were moderate to strong positive.

N/A = Not Applicable

Table J. BioPlex 2200 vs. pANCA IFA – Retrospective Anti-MPO Positive Samples (N=100)

		BioPlex 2200 Vasculitis Anti-MPO Result								
		Positive	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
pANCA IFA Result	Positive	83	6	89	93.3% (83/89)	86.1%, 96.9%	N/A	N/A	84.0% (84/100)	75.6%, 89.9%
	Negative	10	1	11						
	Total	93	7	100						

N/A = Not Applicable

Table K. BioPlex 2200 vs. cANCA IFA – Retrospective Anti-PR3 Positive Samples (N=100)

		BioPlex 2200 Vasculitis Anti-PR3 Result								
		Positive	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
cANCA IFA Result	Positive	93	5	98	94.9% (93/98)	88.6%, 97.8%	N/A	N/A	93.0% (93/100)	86.2%, 96.6%
	Negative	2	0	2						
	Total	95	5	100						

N/A = Not Applicable

Tables L and M compare EIA results from the retrospective positive samples for anti-MPO EIA (N=100) and anti-PR3 EIA (N=100) with ANCA IFA results.

Table L. pANCA IFA vs. Anti-MPO EIA – Retrospective Anti-MPO Positive Samples (N=100)

		Anti-MPO EIA Result									
		Positive	Equivocal*	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
pANCA IFA Result	Positive	87	1	1	89	97.8% (87/89)	92.2%-99.4%	N/A	N/A	87.0% (87/100)	79%, 92.2%
	Negative	11	0	0	11						
	Total	98	1	1	100						

** One (1) anti-MPO EIA equivocal result is included in the Overall Agreement.*

N/A = Not Applicable

Table M. cANCA IFA vs. Anti-PR3 EIA – Retrospective Anti-PR3 Positive Samples (N=100)

		Anti-PR3 EIA Result									
		Positive	Equivocal*	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval	Overall % Agreement	95% Confidence Interval
cANCA IFA Result	Positive	78	10	10	98	79.6% (78/98)	70.6%, 86.4%	N/A	N/A	79.0% (79/100)	70.0%-85.8%
	Negative	1	0	1	2						
	Total	79	10	11	100						

** Ten (10) anti-PR3 EIA equivocal results are included in the Overall Agreement.*

N/A = Not Applicable

A combined positive agreement of 94.1% (176/187) was observed between BioPlex 2200 Vasculitis anti-MPO/anti-PR3 and ANCA IFA results (from Tables L and M), compared to a combined positive agreement of 88.2% (165/187) between anti-MPO/anti-PR3 EIA and ANCA IFA results (from Tables N and O). Also, a combined overall agreement of 88.5% (177/200) was observed between BioPlex 2200 Vasculitis anti-MPO/anti-PR3 and ANCA IFA results compared to a combined overall agreement of 83.0% (166/200) observed between anti-MPO/anti-PR3 and ANCA IFA results.

Table N summarizes the test results (positive percent agreement, negative percent agreement and overall percent agreement) for each of the three antibodies (anti-MPO, anti-PR3 and anti-GBM) from normal blood donors (N=293), unselected patient samples previously tested with vasculitis tests (N=300), and retrospective positive samples (N=100 for anti-MPO, N=100 for anti-PR3 and N=27 for anti-GBM). These sample populations were tested by the BioPlex 2200 Vasculitis kit and anti-MPO, anti-PR3 and anti-GBM EIAs. In addition, anti-MPO and anti-PR3 known positive samples were tested by an ANCA IFA method.

Table N. Summary of Positive, Negative and Overall Percent Agreement for Normal Blood Donors (N=293), Unselected Patient Samples Previously Tested With Vasculitis Tests (N=300), and Retrospective Positive Samples (N=100 for anti-MPO, N=100 for anti-PR3 and N=27 for anti-GBM)

		Anti-MPO EIA Result			pANCA IFA Result			Anti-PR3 EIA Result			cANCA IFA Result			Anti-GBM EIA Result		
		% Pos Agreement	% Neg Agreement	% Overall Agreement	% Pos Agreement	% Neg Agreement	% Overall Agreement	% Pos Agreement	% Neg Agreement	% Overall Agreement	% Pos Agreement	% Neg Agreement	% Overall Agreement	% Pos Agreement	% Neg Agreement	% Overall Agreement
BioPlex 2200 Vasculitis Result	Normal Blood Donors*	N/A	293/293 100.0%	293/293 100.0%	NT	NT	NT	N/A	293/293 100.0%	293/293 100.0%	NT	NT	NT	N/A	289/291 99.3%	289/293 98.6%
	Unselected Patient Samples Previously	5/7 71.4%	284/291 97.6%	289/300 96.3%	NT	NT	NT	5/5 100.0%	292/295 99.0%	297/300 99.0%	NT	NT	NT	Not Accurate (0/1)	298/299 99.7%	298/300 99.3%
	Retrospective Positive Samples	92/98 93.9%	N/A	93/100 93.0%	83/89 93.3%	N/A	84/100 84.0%	79/79 100.0%	N/A	83/100 83.0%	93/98 94.9%	N/A	93/100 93.0%	16/18 88.9%	N/A	25/27 92.6%

* *Normal blood donors and unselected patient samples previously tested with vasculitis tests were not tested by ANCA IFA.*

N/A = Not Applicable

NT = Not Tested

E. Cross-Reactivity

A cross-reactivity study was performed to determine if samples from various disease states and other potentially interfering factors interfere with test results when tested with the BioPlex 2200 Vasculitis kit. A panel of ten (10) specimens positive for each cross reactant were evaluated for possible cross reactivity with the BioPlex 2200 Vasculitis kit for each of the three (3) autoantibodies. Samples were also tested on a corresponding commercially available microplate EIAs. Most of the samples evaluated were high positive for each disease state. The results demonstrated that the various disease state samples evaluated do not cross react with the three (3) autoantibodies in the BioPlex 2200 Vasculitis kit. Results can be found in the below table:

Table. Cross-Reactivity

Cross Reactives	N	Method	Anti-MPO	Anti-PR3	Anti-GBM
ANA	10	BioPlex 2200	0	0	0
		EIA	0	0	0
		Discrepants	0	0	0

Anti-Saccharomyces Cerevisiae (ASCA)	10	BioPlex 2200	0	1	0
		EIA	0	1	0
		Discrepants	0	0	0
Anti-Cardiolipin	10	BioPlex 2200	0	0	0
		EIA	1	0	0
		Discrepants	1	0	0
Anti-dsDNA	10	BioPlex 2200	0	0	0
		EIA	0	0	0
		Discrepants	0	0	0
Anti-Histone	10	BioPlex 2200	2	2	0
		EIA	1	0	0
		Discrepants	1	2	0
Rheumatoid Factor (RF)	10	BioPlex 2200	0	0	0
		EIA	0	0	0
		Discrepants	0	0	0
Anti-Thyroid Peroxidase (TPO)	10	BioPlex 2200	0	0	0
		EIA	0	0	0
		Discrepants	0	0	0
Anti-tissue Transgluta-minase (tTG)	7*	BioPlex 2200	0	0	0
		EIA	0	0	0

		Discrepants	0	0	0
Anti-Smooth Muscle (ASMA)	10	BioPlex 2200	0	0	0
		EIA	0	0	0
		Discrepants	0	0	0
HCV	10	BioPlex 2200	0	0	0
		EIA	0	0	0
		Discrepants	0	0	0
HIV	10	BioPlex 2200	0	0	0
		EIA	0	0	0
		Discrepants	0	0	0

** Due to limited availability of samples, only seven tTG specimens were evaluated.*

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

OCT 31 2007

Bio-Rad Laboratories
c/o Ms. Priya Bondre
Regulatory Affairs Representative
6565 185th Avenue NE
Redmond, WA 98052

Re: k072358
Trade/Device Name: BioPlex™ 2200 Vasculitis kit
BioPlex™ 2200 Vasculitis Calibrator Set
BioPlex™ 2200 Vasculitis Control Set
Regulation Number: 21 CFR 866.5660
Regulation Name: Multiple Autoantibodies Immunological Test System
Regulatory Class: Class II
Product Code: MOB, MVJ, JIX, JJY
Dated: August 20, 2007
Received: August 22, 2007

Dear Ms Bondre:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket

notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Robert L. Becker, Jr., M.D., Ph. D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number: K072358

Device Name: BioPlex™ 2200 Vasculitis kit on the BioPlex™ 2200 Multi-Analyte Detection System
BioPlex™ 2200 Vasculitis Calibrator Set
BioPlex™ 2200 Vasculitis Control Set

Indications For Use:

BioPlex™ 2200 Vasculitis kit

The BioPlex™ 2200 Vasculitis kit is a multiplex flow immunoassay intended for the semi-quantitative detection of IgG autoantibodies to Myeloperoxidase (MPO), serine Proteinase 3 (PR3) and Glomerular Basement Membrane (GBM) in human serum.

The BioPlex 2200 Vasculitis kit is intended for use with the Bio-Rad BioPlex 2200 System.

Uses:
The test system is used to detect the presence of antibodies in serum samples, as an aid in the diagnosis of certain autoimmune vasculitides such as Microscopic Polyangiitis (MPA), Necrotising Glomerulonephritis, Churg-Strauss Syndrome, Wegener's Granulomatosis and autoimmune renal disorders, such as Goodpasture's syndrome, in conjunction with clinical findings and other laboratory tests.

BioPlex™ 2200 Vasculitis Calibrator Set

The BioPlex 2200 Vasculitis Calibrator Set is intended for the calibration of the BioPlex 2200 Vasculitis Reagent Pack.

BioPlex™ 2200 Vasculitis Control Set

The BioPlex 2200 Vasculitis Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 Instrument and BioPlex 2200 Vasculitis Reagent Pack in the clinical laboratory. The performance of the BioPlex 2200 Vasculitis Control Set has not been established with any other Vasculitis assays.

Prescription Use ✓ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Maria M Chan
Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K072358